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10/507,389	01/20/2005	Yuko Aoki	18201-002US1	1796

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/507,389	AOKI ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *6,7,10-20 and 24-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-9,21-23,32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 6/16/08, are acknowledged. Amended claims 1-3, 5, 8, 23, and new claims 32-36 are acknowledged. Claims 24-31 remain withdrawn from consideration as being drawn to non-elected Groups. Claims 6-7 and 10-20 remain withdrawn from consideration as being drawn to non-elected species.

Applicant's arguments, filed 6/16/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-5, 8-9, 21-23, and 32-36 are herein under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5, 8-9, 21-23, and 32-36 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. This rejection is maintained for claims 1-5, 8-9, 21-23, necessitated by amendment for claims 32-36 and reiterated for reasons of record.

Under the Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility (published in the O.G. notice (1300 OG 142) on 11/22/2005) a method that

does not result in a physical transformation of matter MAY be statutory where it recites a concrete, tangible and useful result; i.e. a practical application.

Claims 1-5, 8-9, 21-23, and 32-36 are drawn to a method for constructing a model that predicts sensitivity to a drug based on the expression levels of genes. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

In the instant case, claims 1-5, 8-9, 21-23, and 32-36 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. The method as claimed may take place entirely within the confines of a computer without any communication to the outside world. It is noted that claim 1 recites "making a model available"; however, this limitation does not address to what or whom the model is made available. It is noted that one embodiment of this limitation reasonably includes making the model available in the computer which does not represent any communication to the outside

world. It is noted that claim 33 recites "storing a description of the model on a data storage device or displaying the description of the model on a display screen". While "displaying the description of the model on a display screen" is statutory subject matter, the claim is written in the alternative with the "storing" limitation encompassing an embodiment that is nonstatutory subject matter. This is because storing a description on a data storage device may result in the description being confined in the computer and does not necessarily mean that the results are intended to be "presented" in some tangible form to a user. Because no practical result is recited in the claims, these instant claims do not include any tangible result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a user, or by including a physical transformation (provided there is adequate written support in the originally filed application).

Applicant argues that the non-statutory subject matter rejection should be withdrawn because amended claim 1 recites the model is made available to estimate the sensitivity. This statement is found unpersuasive as this limitation does not address to what or whom the model is made available. It is noted that one embodiment of this limitation reasonably includes making the model available in the computer which does not represent any communication to the outside world.

Claim Rejections - 35 USC § 112, First paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-9, 21-23, and 32-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

NEW MATTER

Applicant did not point to any written support in the originally filed application for the claim amendments. There does not appear to be adequate written support for the limitations: "making said model available to estimate the sensitivity of the biological specimen to the specific drug" (claim 1) and "selecting those models in which the number of genes is smaller than the number of genes in other models, those models whose square of the predictive correlation coefficient (Q^2) value is higher than the Q^2 values of other models, or those models in which the number of genes is smaller than the number of genes in other models and whose Q^2 value is higher than the Q^2 values of other models" (claim 2).

While the specification recites predicting drug sensitivity based on the model (abstract), this passage does not provide adequate written support for "making said model available" which differs in scope. While the specification recites "selecting a model with the smallest number of genes and/or highest Q^2 value" (page 34, lines 15-20), this passage differs from the amended limitation in claim 2 which is broader in scope.

Because the limitations "making said model available to estimate the sensitivity of the biological specimen to the specific drug" (claim 1) and "selecting those models in which the number of genes is smaller than the number of genes in other models, those models whose square of the predictive correlation coefficient (Q^2) value is higher than the Q^2 values of other models, or those models in which the number of genes is smaller than the number of genes in other models and whose Q^2 value is higher than the Q^2 values of other models" (claim 2) do not appear to have adequate written support in the specification, claims, and/or drawings, as originally filed, these limitations are considered to be NEW MATTER. Claims 3-5, 8-9, 21-23, and 32-36 are also rejected due to their dependency from claims 1 and 2. This rejection is necessitated by amendment.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 8-9, 21-23, and 32-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1 (line 8) and 34 (line 2) recite the limitation "using" which is vague and indefinite. It is unclear what step or steps are encompassed by this limitation. Clarification of this issue via clearer claim wording is requested. Claims 2-5, 8-9, 21-23 are also rejected due to

their dependency from claim 1. This rejection is maintained for claims 1-5, 8-9, and 21-23 and necessitated by amendment for claims 32-36.

Applicant argues that one of ordinary skill would know how a model can be constructed by a PLS method type 1 "using" sensitivity data and gene expression data and has submitted pages 293-359 from the Martens et al. book showing the "used" term. This statement is found unpersuasive because while Martens et al. give an example of "using", it is still unclear what step or steps are encompassed by this limitation in claims 1 and 34.

Claim 3 (lines 6-7) recites the limitation "relatively greater contributions" which is incomplete because the limitation is a relative one with no frame of reference given. Clarification of this issue via clearer claim wording is requested. Claim 4 is also rejected due to its dependency from claim 3. This rejection is necessitated by amendment.

Claim 36 recites "reflects the responsiveness" which is vague and indefinite. It is unclear what Applicant intends this term to mean. It is unclear if "reflects" is intended to mean "show" or to mirror (which could result in the opposite of what is actually present) or exhibit as an image or some other scenario. Clarification of this issue via clearer claim wording is requested. This rejection is necessitated by amendment.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 5, 8, 21, 23, 34, and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Rocke et al. (US 2002/0111742 A1). This rejection is maintained for claims 1, 2, 5, 8, 21, 23, and necessitated by amendment for claims 34 and 36 and reiterated for reasons of record.

Rocke et al. disclose a method for generating a model for predicting the classification of a biological sample using partial least squares (PLS) and determining an estimated conditional class probability of the prediction (0009, 0015, 0017, 0039, 0048, claim 2) and using gene expression data to predict patient survival, drug sensitivity of a tumor, or other clinical outcomes (0146), as stated in the preamble of instant claim 1. Rocke et al. disclose using samples (0023, 0044, 0049), obtaining data from a biological sample including gene expression measurements and ratios between a reference and test measurement, using univariate PLS (type I) (abstract, 0016, 0080, 0084, 0111), constructing PLS components to maximize covariance between the response variable and a linear combination of predictors (0032), with p predictor values and y denoting a binary response value (i.e. y=0 for normal sample, y=1 for a tumor sample and x is the corresponding expression values of p genes) (0038), and each sample has a response variable y (claim 1) that identify a G group (i.e. different reactions to drug therapy, predicted survival times; claims 17 and 19) (sensitivity data) and the combination of the predictor (gene expression) values (X) such that an estimation of sensitivity can be made in classifying the sample (0032, 0048, claims 1, 3, 13, 14, 16, 17, and 19), and generating a model (0009, 0015), as stated in

instant claim 1) as well as estimating the sensitivity (0009, and wherein survival times represent clinical sensitivity data (as stated in instant claim 8) as well as estimating the sensitivity (0009, 0039, 0048, claims 2, 17) (as stated in instant claims 34 and 36). Rocke et al. disclose generating different combinations of genes based on a genetic algorithm (0098), and selecting models in which the number of genes is smaller than that of other models using PLS (0009, 0016, 0018, 0023, 0024, 0026, 0039, 0044-0046, 0050, 0088, 0091), as stated in instant claims 2 and 5. Rocke et al. disclose high density nucleic acid array data that correlate sensitivity of a cell to a drug (0005, 0111, 0146) and analysis procedures for the prediction of biological samples, such as human tumor samples, based on high dimensional data obtained from microarray gene expression measurements (0005, 0016, 0055), as stated in instant claims 21 and 23.

Thus, Rocke et al. anticipate the limitations of instant claims 1, 2, 5, 8, 21, 23, 34, and 36.

Applicant summarizes instant claim 1. Applicant summarizes PLS-1 and PLS-2. Applicant argues that Rocke et al.'s multi-class classification is understood to use partial least squares method type 2. This statement is found unpersuasive as Rocke et al. use univariate and multivariate PLS (i.e. 0111). It is noted that univariate PLS is PLS-1 (also known as type 1) (i.e. see Garthwaite publication (cited in Rocke et al. application in paragraphs 0150, 0192)).

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8, 21-23, and 32-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rocke et al. (US 2002/0111742 A1) in view of Kovesdi et al. (US 2004/0199334 A1). This rejection is maintained for claims 1-5, 8, 21-23 and necessitated by amendment for claims 32-36 and reiterated for reasons of record.

Rocke et al. describe the limitations of claims 1, 2, 5, 8, 21, 23, 34, and 36 as stated in the 35 USC 102 rejection above. Rocke et al. do not describe selecting models whose Q^2 value is higher than Q^2 values of other models (instant claim 2), computing a parameter representing degree of contribution and selecting the genes that make relatively greater contributions (instant claim 3), a modeling power value (instant claim 4), an anti-tumor effect (instant claim 22),

machine-readable data (instant claim 32), storing or displaying a model description (instant claim 33), storing the sensitivity estimate (instant claim 35).

Kovesdi et al. describe a method for providing a model for generating a quantitative structure property activity relationship (QS(P)AR) (abstract) and the prediction of biological activity and physico-chemical properties of compounds (0001, 0017, 0126). Kovesdi et al. describe establishing biological/physical/chemical data providing a model involving partial least squares, selecting significant descriptors according to their influence to the property activity relationship, and verifying the model by use of a quality parameter (claims 1, 7). Kovesdi et al. describe the QS(P)AR can be performed by applying partial least squares (PLS) algorithm to achieve an optimal quality parameter (0051), and model fitting with Q^2 value (square of the predictive correlation coefficient) of model predictions of 0.4 or higher for use as a reliable prediction of biological activity and properties (0070, 0048-0049, 0054, 0056, 0118-0123, 0126-0127), as stated in instant claim 2. Kovesdi et al. describe establishing a set of minimal important descriptors (0014). Kovesdi et al. describe selecting via genetic algorithms (claim 8), as stated in instant claim 5. Kovesdi et al. describe calculating the absolute values of the descriptors coefficients (parameter) to quickly quantify the importance of the descriptors in the model that estimates predictive ability of the model and evaluates sensitivity and remove descriptors with lowest importance (i.e. selecting the descriptors that have greater relative contributions) (0125-0127) as well as optimal relationships from maximum validated prediction power and achieving an optimal quality parameter (0051, 0132) which represents computing a parameter that represents degree of contribution and selecting descriptors with relatively greater contributions (as stated in instant claim 3) and modeling power value (as stated in instant claim

4). Kovesdi et al. describe analysis of tumor dihydrofolate reductase inhibitors (Example 1) which represents an antitumor effect, as stated in instant claim 22. Kovesdi et al. describe machine readable data (claims 16 and 26; 0071, 0072), as stated in instant claim 32. Kovesdi et al. describe storing and displaying a model description and storing an sensitivity estimate (claims 16 and 26; 0025, 0071, 0127, 0140), as stated in instant claims 33, 34, and 35.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to fit a Q^2 value (square of the predictive correlation coefficient) as taught by Kovesdi et al. into the drug predictive model method of Rocke et al. wherein the motivation would have been to correlate large volumes of data to a biological response and extract meaningful information from data such as predicting the biological state of a sample which in turn would improve the ability to apply genomics data to improve medical diagnoses and treatments, as taught by Rocke et al. (0005).

Thus, Rocke et al., in view of Kovesdi et al., make obvious claims 1-5, 8, 21-23, and 32-36.

Applicant argues that Rocke et al.'s multi-class classification is PLS-2 and would not lead to constructing a model that estimates sensitivity of a biological specimen to a specific drug by PLS method type 1. This statement is found unpersuasive as Rocke et al. use univariate and multivariate PLS (i.e. 0111). It is noted that univariate PLS is PLS-1 (also known as type 1). Applicant argues that Kovesdi et al. do not remedy the deficiencies of Rocke et al. This statement is found moot as Rocke et al. address the PLS type 1 limitation, as discussed above.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. If you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, please call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

September 8, 2008

/Carolyn Smith/
Primary Examiner
AU 1631